

# FEE TRANSMITTAL for FY 2003

Effective 01/01/2003. Patent fees are subject to annual revision.

☒ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT

(\$)

## Complete if Known

Application Number 09/900,497

Filing Date July 6, 2001

First Named Inventor KEITH D. ALLEN

Examiner Name Celine X. Qian

Art Unit 1636

Attorney Docket No. R-639

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## METHOD OF PAYMENT (check all that apply)

☐ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☒ Deposit Account:

Deposit Account Number  
Deposit Account Name

50-1271

Deltagen, Inc.

The Commissioner is authorized to: (check all that apply)

☒ Charge fee(s) indicated below ☐ Credit any overpayments

☐ Charge any additional fee(s) during the pendency of this application

☐ Charge fee(s) indicated below, except for the filing fee to the above-identified deposit account.

## FEE CALCULATION

### 1. BASIC FILING FEE

Large Entity Fee Code (\$)	Small Entity Fee Code (\$)	Fee Description	Fee Paid
1001 750	2001 375	Utility filing fee	
1002 330	2002 165	Design filing fee	
1003 520	2003 260	Plant filing fee	
1004 750	2004 375	Reissue filing fee	
1005 160	2005 80	Provisional filing fee	

SUBTOTAL (1) (\$)

### 2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

Total Claims	Extra Claims	Fee from below	Fee Paid
Independent Claims	-20** =	X	
Multiple Dependent	-3** =	X	

Large Entity Fee Code (\$)	Small Entity Fee Code (\$)	Fee Description
1202 18	2202 9	Claims in excess of 20
1201 84	2201 42	Independent claims in excess of 3
1203 280	2203 140	Multiple dependent claim, if not paid
1204 84	2204 42	** Reissue independent claims over original patent
1205 18	2205 9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) (\$)

\*\*or number previously paid, if greater; For Reissues, see above

## FEE CALCULATION (continued)

### 3. ADDITIONAL FEES

Large Entity Fee Code (\$)	Small Entity Fee Code (\$)	Fee Description	Fee Paid
1051 130	2051 65	Surcharge - late filing fee or oath	
1052 50	2052 25	Surcharge - late provisional filing fee or cover sheet	
1053 130	1053 130	Non-English specification	
1812 2,520	1812 2,520	For filing a request for ex parte reexamination	
1804 920*	1804 920*	Requesting publication of SIR prior to Examiner action	
1805 1,840*	1805 1,840*	Requesting publication of SIR after Examiner action	
1251 110	2251 55	Extension for reply within first month	
1252 410	2252 205	Extension for reply within second month	
1253 930	2253 465	Extension for reply within third month	465.00
1254 1,450	2254 725	Extension for reply within fourth month	
1255 1,970	2255 985	Extension for reply within fifth month	
1401 320	2401 160	Notice of Appeal	
1402 320	2402 160	Filing a brief in support of an appeal	
1403 280	2403 140	Request for oral hearing	
1451 1,510	1451 1,510	Petition to institute a public use proceeding	
1452 110	2452 55	Petition to revive - unavoidable	
1453 1,300	2453 650	Petition to revive - unintentional	
1501 1,300	2501 650	Utility issue fee (or reissue)	
1502 470	2502 235	Design issue fee	
1503 630	2503 315	Plant issue fee	
1460 130	1460 130	Petitions to the Commissioner	
1807 50	1807 50	Processing fee under 37 CFR 1.17(q)	
1806 180	1806 180	Submission of Information Disclosure Stmt	
8021 40	8021 40	Recording each patent assignment per property (times number of properties)	
1809 750	2809 375	Filing a submission after final rejection (37 CFR 1.129(a))	
1810 750	2810 375	For each additional invention to be examined (37 CFR 1.129(b))	
1801 750	2801 375	Request for Continued Examination (RCE)	
1802 900	1802 900	Request for expedited examination of a design application	

Other fee (specify)

\*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) (\$ 465.00)

## SUBMITTED BY

Name (Print/Type)	Aaron T. Hokamura	Registration No. (Attorney/Agent)	51,810	Telephone	650-569-5171
Signature		Date	March 10, 2003		

**WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.**

This collection of information is required by 37 CFR 1.17 and 1.27. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Washington, DC 20231.

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7 2003

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**TRANSMITTAL  
FORM**

(to be used for all correspondence after initial filing)

Application Number	09/900,497
Filing Date	July 6, 2001
First Named Inventor	KEITH D. ALLEN
Art Unit	1636
Examiner Name	Celine X. Qian
Attorney Docket Number	R-639


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Total Number of Pages in This Submission

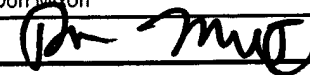
**ENCLOSURES (Check all that apply)**

<input checked="" type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input checked="" type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input checked="" type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Response to Missing Parts/Incomplete Application <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation <input type="checkbox"/> Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____	<input type="checkbox"/> After Allowance Communication to Group <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input type="checkbox"/> Other Enclosure(s) (please identify below):
Remarks		

**SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT**

Firm or Individual	Aaron T. Hokauma, Reg. No. 51,810
Signature	
Date	March 10, 2003

**CERTIFICATE OF TRANSMISSION/MAILING**

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231 on this date: <u>March 10, 2003</u>			
Typed or printed	Don Mixon		
Signature		Date	March 10, 2003

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Washington, DC 20231.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/900,497	07/06/2001	Keith D. Allen	R-639	4128

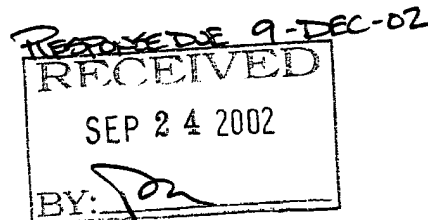
7590 09/09/2002  
DELTAGEN, INC.  
1003 Hamilton Avenue  
Menlo Park, CA 94025

EXAMINER	
QIAN, CELINE X	
ART UNIT	PAPER NUMBER
1636	12

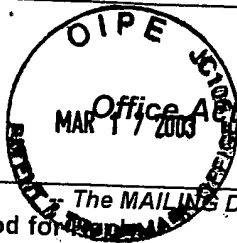
DATE MAILED: 09/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

DUE: DEC. 9, 02



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Office Action Summary

Application No.	Applicant(s)	
09/900,497	ALLEN, KEITH D.	
Examiner	Art Unit	
Celine Qian	1636	

Period for Reply: The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 August 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 16-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

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Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

### DETAILED ACTION

Claims 1-20 are pending in the application.

#### *Election/Restrictions*

Applicant's election with traverse of Group I in Paper No. 11 is acknowledged. The traversal is on the ground(s) that the inventions of Groups I, II and II related, thus a search of all the groups can be made without serious burden. However, the Applicant does not offer any support for this assertion. This is not found persuasive because the inventions are patentably distinct for the reasons set forth of the record mailed on 7/2/02. A search of the subject matter of one invention would not be co-extensive with a search of the other invention, and therefore the additional search effort involved in searching all three inventions in a single application would be burdensome. Each invention is capable of supporting a separate patent.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 16 and 20 are withdrawn from consideration as being directed to non-elected subject matter. Claims 1-15 and 17-19 are currently under examination.

#### *Claim Objections*

Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim is drawn to a construct comprising a screening marker. Since it's unclear how it is different from the "selection marker," claim 2 fails to limit the subject matter of claim 1.

→ p. 14 line 16 - 18  
p. 11, line 25-27

*Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The nature of the invention is a method of identifying an agent that modulates the NPY6 receptor gene expression and function by administering an agent to a NPY6 receptor gene knockout animal, and determine whether the expression or function of NPY6 receptor gene is modulated.

The guidance in the specification is limited in regarding this method. The specification does not teach a specific method in determining the expression or function of NPY6 receptor in a NPY6 receptor knockout animal. It is not known how to determine the expression or function of a gene that has already been knocked out. The prior art does not teach such a method either. In view of lack of guidance from both specification and prior art, one skilled in the art would have to engage in undue amount of experimentation to practice the method as claimed. If this aspect of rejection can be overcome, the scope of enablement rejection set forth below is applicable.

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Claims 5-10, 17-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, [while being enabling for a homozygous knockout mouse comprising a disruption in the NPY6 receptor gene comprising the sequence set forth in (SEQ ID NO:1), wherein both alleles are inactivated, and exhibiting phenotypic features such as increased agility or coordination as compared to wild type mice, a method of producing such a transgenic mouse, and a method of identifying an agent that modulates the expression and/or function of NPY6 gene, and a cell isolated from the KO mouse] does not reasonably provide enablement for other transgenic and/or knockout animal comprising any disruption in any NPY6 receptor homolog gene. Further, the specification is not enabling for a knockout mouse comprising any disruption in any NPY6 receptor homolog gene and for any cell comprising any disruption in a NPY6 receptor homolog gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the Invention:

Claims 5-10, 17-19 are drawn to a cell comprising a disruption in a NPY6 receptor homolog gene, a non-human transgenic animal comprising a disruption in a NPY6 receptor homolog gene, a cell from that transgenic animal, a method of producing the mouse with any disruption in the said gene, and a method of identifying an agent having an effect on a phenotype associated with the transgenic mouse. Thus, the nature of the invention is directed to transgenic animals and methods of using the transgenic animals in identifying agents that modulate gene expression.

Breadth of Claims:

In the instant case, the claims 5-10, 17-19 encompass any transgenic animal containing any disrupted allele for the gene that encodes any NPY6 receptor homolog. Further, the claims encompass any knockout mouse comprising any disruption in NPY6 receptor homolog gene and exhibiting the phenotypes of increased agility or coordination as compared to wild type mice. Further, the claims encompass any cell comprising any disruption in a NPY6 receptor homolog gene and encompass all cells capable of undergoing homologous recombination (specification page 9, line 1-3). The disruption, as disclosed in the specification (page 8, line 21-29) includes any insertion, deletion or substitution in any portion of the gene (introns, exons, regulatory regions). The claims, therefore, encompass all such disruptions and also cover all animals that contain NPY6 receptor homolog gene disruption (page 9, lines 1-3).

The specification does not provide an enabling disclosure for the full scope of transgenic animals of the type claimed. The only embodiment enabled by the specification within the scope of claims 5-10, 17-19 is for a homozygous knockout mouse comprising a disruption in the NPY6 receptor gene that results in loss of function of the NPY6 receptor gene and exhibiting



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phenotypic features such as increased agility or coordination as compared to wild type mice, a method of producing such a transgenic mouse. Thus the breadth of claims is very broad and encompasses any transgenic animal and a knockout mouse with any disruption in any NPY6 receptor gene and includes any and all mutant forms, substitutions, deletions, or insertions in any NPY6 receptor gene (specification, page 7, lines 15-23).

Amount of guidance in the specification and Working Examples:

The specification discloses the use of a specific NPY6 receptor gene as set forth in SEQ ID NO:1 in producing a homozygous transgenic knockout mouse, wherein the knockout mouse exhibits phenotypic changes that include increased agility or coordination as compared to wild type mice.

The specification and the working examples provide sufficient guidance to practice the invention with only a homozygous, knockout mouse containing two disrupted alleles for the gene that encodes a murine NPY6 receptor gene of SEQ ID NO:1 wherein the disruption results in loss of function of the NPY6 receptor gene. The specification does not teach how to make and use the invention with other species of transgenic or knockout animals and with any knockout mouse with any form of disruption in the gene encoding NPY6 receptor, as claimed in the claims 5-15, 17-19. Further, the specification does not teach how to make and use any cell comprising any type of disruption in a NPY6 receptor gene as claimed. The scope of claims 5-10, 17-19 thus surpasses that enabled by the specification.

State of the Art, Predictability or Unpredictability of the art, Amount of experimentation necessary and Skill level of the artisan:

Although the skill of an artisan in this subject area is considered to be very high, it would require undue experimentation on the part of an artisan to make and use the claims as specified and use the invention with any and all transgenic animals as claimed. The specification and the working examples provide sufficient guidance to practice the invention with only a homozygous, knockout mouse containing two disrupted alleles for the gene that encodes a murine NPY6 receptor wherein the knockout mice exhibit increased agility or coordination. However, neither the specification nor the working examples provide enough guidance on how to practice the invention with any and all transgenic animals and/or transgenic mice carrying any and all transgene(s) of the types recited in the claims.

When considering the predictability of this invention, one has to remember that many of the phenotypes examined in transgenic and knockout models are influenced by the genetic background in which they are studied and the effect of allelic variation and the interaction between the allelic variants (pg. 1425, paragraph 1 in Sigmund, C.D. 2000. *Arterioscler Thromb Vasc Biol.* 20:1425-1429). The specification discloses the phenotype of a homozygous NPY6 receptor gene knockout mouse comprising a disruption in the NPY6 receptor gene comprising the sequence set forth in SEQ ID NO:1 and fails to disclose the phenotypes of any and all KO animals with a disruption in NPY6 receptor gene. Thus, the phenotype of any transgenic or knockout animal is unpredictable. Thus, the specification, in the instant case, is not enabling for transgenic and/or knock out animals, including mice, that exhibit no phenotype or that exhibit transgene-dependent phenotypes other than that disclosed in the instant specification.

Further, the transgene expression and the physiological consequences of transgene products are not always accurately predicted in transgenic mouse studies (pg. 62, paragraph 1,

lines 7-9 in Wall, R.J. 1996. *Theriogenology* 45:57-68). Thus, the invention while being enabled for a homozygous knockout mouse containing two disrupted alleles for the gene comprising the sequence set forth in SEQ ID NO:1 and encodes a NPY6 receptor, does not extend the predictability of the invention to other animal systems.

The particular genetic elements required for expression varies from species to species. Our lack of understanding of essential genetic control elements makes it difficult to design transgenes with predictable behavior (Wall, 1996). Therefore, the phenotype of knockout animals is not always predictable. For example, Jacks et al. (1992) describe Rb KO mice that do not display retinoblastoma; rather they exhibit the unexpected phenotype of pituitary tumors. The pituitary tumors arise from cells lacking a wild-type Rb allele. Thus, tumors were found to arise not in retinas, as in humans, but in the pituitary gland (page 299, Discussion, paragraphs 1 and 3). Therefore, in the absence of specific guidance and working examples, the production of transgenic animals with the scope as claimed is unpredictable. In such a situation, one skilled in the art would not know how to make and use the invention as claimed, without undue experimentation.

The specification fails to provide an enabling disclosure for the preparation of other species of knockout animals besides mice having a disruption in the NPY6 receptor gene because the guidance offered in the specification is limited to the preparation of mice harboring such mutations and no teachings or guidance are offered in regard to how one would have prepared any other type of animal having the recited gene disruption. Since homologous recombination is required for gene targeting methods such as employed in the instant invention, embryonic stem (ES) cell technology must be available to carry out the method. The only species in which such

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technology was known was the mouse and the artisan did not accept that it was possible to have prepared ES cells in other species (see e.g. Bradley et al., paragraph bridging pages 537-538). Campbell and Wilmut, 1997 acknowledge reports of ES-like cell lines in a number of species, but emphasize that as yet there are no reports of any cell lines which contribute to the germ line in any species other than the mouse (p. 65). Likewise, Mullins et al. (1996) teach that "[a]lthough to date chimeric animals have been generated from several species including the pig, in no species other than the mouse has germline transmission of an ES cell been successfully demonstrated. This remains a major goal for the future and may well require the use of novel strategies which depart widely from the traditional methods used in the mouse" (p. S38, column 1, paragraph 1. Thus, knockout animals cannot be prepared for any species other than the mouse. Since ES cell technology was required to produce the claimed animals and practice the claimed methods of using such animals, in the absence of such technology available in other species, one skilled in the art would have been required to exercise undue experimentation to produce the claimed animals and to practice of the claimed methods in species other than mice.

In view of the limited guidance in the specification, and limited working examples directed to transgenic, knockout mice with a specific knockout gene and exhibiting a specific phenotype, and the unpredictability of the art, one skilled in the art would be required to engage in undue experimentation, in order to make and use the invention in its full scope as claimed. Thus, the enabled scope of the claims is limited to a homozygous knockout mouse comprising a disruption in the NPY6 receptor gene as set forth in SEQ ID NO:1 and exhibiting phenotypic features of increasing agility or coordination as compared to wild type mice, and a method of producing such a transgenic mouse.

Claims 17 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants are referred to the guidelines on written description published January 5, 2001 in the Federal Register at Volume 66, No. 4, pp. 1099-1111 (also available at [www.uspto.gov](http://www.uspto.gov)).

The specification does not provide or point to a written description of the genus of NPY6 receptor genes recited in the claims. Claims 17 is directed to a transgenic and/or knockout mouse containing NPY6 receptor or homology gene disruption. However, the specification only describes a single species of a transgenic, knockout mouse of the type claimed, wherein the said disruption is within the gene that encodes a specific NPY6 receptor gene comprising the SEQ ID No:1. The specification fails to teach other "homolog" of SEQ ID NO:1 from other species of animals besides mice, or "homolog" that has the same function as murine NPY6 receptor. In analyzing whether a written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, the claims encompass the whole genus of 'NPY6 receptor or homolog genes' and include any and all transgenic animals that contain any altered allele for the gene that encodes a NPY6 receptor or a homology thereof. Thus for the claims to meet the written description requirement, other representative species of "NPY6 receptor homolog genes", should be described by their complete structure or by other relevant identifying characteristics, in the specification.

Next, then, it is determined if a representative number of species have been sufficiently described by other relevant identifying characteristics. In the instant case, no identifying characteristics are provided for the genus of NPY6 receptor homolog gene disruptions recited in the claims. Thus the limited information in the specification is not deemed sufficient to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed genus of NPY6 receptor homolog gene disruptions. Thus, it is concluded that the written description requirement is not satisfied for the claimed genus of "NPY6 receptor or homolog genes".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1-4 and 10, it is unclear how the target construct is arranged. In other words, is the first polynucleotide adjacent to the second polynucleotide or there is a selectable marker in between? Where is the screening marker located in the construct? In addition, it is also unclear whether the first and second polynucleotide is a contiguous sequence of the target gene or just portions of the target gene.

Regarding claim 2, the term "screening marker" renders the claim indefinite because it is unclear what term encompasses. In other words, it is unclear how a "screening marker" differs from the "selection marker" recited in claim 1.

Regarding claim 9, the word "derived" renders the claim indefinite because the nature and number of derivative processes is unknown.

*Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mansour et al (1988, Nature, vol. 336, No. 24, 348-352), in view of Weinberg et al. (1996, JBC Vol. 271, pages 16435-16438).

The claims are drawn to an NPY6 receptor gene-targeting construct and a method of making said construct. The claims are further drawn to a cell and a transgenic animal comprising a disruption in an NPY6 receptor, and a method of producing a transgenic mouse comprising a disruption in an NPY6 receptor gene by homologous recombination using the target construct.

Mansour et al. teach a strategy for targeted disruption of the hprt gene and proto-oncogene int-2 in mouse embryonic stem cells and subsequent generation of knockout mice. Their teaching addresses the previous technical difficulty of obtaining embryonic stem cell carrying non-selectable, targeted gene mutation at loci of interest, and therefore provides a model which can be used to produce homozygous mutation of any gene, regardless of its function, if a cloned fragment of the gene is available (see page 348, second paragraph, line 1-3, third paragraph, line 1-5, and page 352, fourth paragraph, line 1-3). Mansour et al. further teach the

generation of two targeting constructs, pRV9.1/TK and pINT-2-N/TK, each contains two sequences from an *hprt* gene and an *int-2* gene respectively, and a neo selection marker gene in between the two sequences (see page 350, figure 3). However, Mansour et al. do not teach how to make a NPY6 receptor target construct and knockout mouse.

Weinberg et al. teach that NPY has various biological function including effects on anxiety, cardiovascular function and feeding behavior; and NPY exerts these varied functions through the interaction with distinct receptor subtypes (see page 16435, 1<sup>st</sup> col., 1<sup>st</sup> and 2<sup>nd</sup> paragraph). Weinberg et al. teach that such receptors are classified into five subtypes based on their pharmacological properties consisting Y1, Y2, Y3, Y4, and "atypical" Y1 (see page 16435, 2<sup>nd</sup> col., lines 1-4). Weinberg et al. further teach the cloning of a new receptor subtype of NPY, Y5 (the sequence deposit number in Gene Bank, U58367 is same as the sequence in SEQ ID NO:1 of the specification although the specification name this receptor Y6), that is expressed specifically in kidney and within the discrete regions of hypothalamus (see Figure 3, and page 16438, 1<sup>st</sup> col., 2<sup>nd</sup> paragraph, lines 7-10). Weinberg et al. further teach the nucleic acid sequence encoding said receptor (see Figure 1, and Gene Bank U58367). Weinberg et al. also teach that inhibiting said receptor by antisense or antibody would help to address the precise physiological role of this receptor.

Based on the teaching of Weinberg et al. that each NPY subtype is involved in specific function of NPY, it would have been obvious to one of ordinary skill in the art to knockout the NPY6 receptor to study what biological role it plays in NPY signaling pathway. The ordinary artisan would have been motivated to knockout the expression of the NPY6 receptor gene in a mouse to study the role it plays in the complex biology of NPY and determine which NPY



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signaling pathway(s) it mediates, as suggested by the teaching of Weinberg et al. The ordinary artisan would have had reasonable expectation of success for making such a knockout mouse because of the teachings of Mansour et al., who teach a general method of targeted gene disruption in mice based on homologous recombination using a cloned fragment of a desired gene, and Weinberg et al., who teach the coding sequence of the mouse NPY6 receptor gene. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

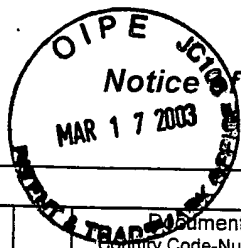
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.  
September 7, 2002

*Anne-Marie Baker*  
ANNE-MARIE BAKER  
PATENT EXAMINER



# Notice of References Cited

Application/Contr. No.

09/900,497

Applicant(s)/Patent Under

Reexamination

ALLEN, KEITH D.

Examiner

Celine Qian

Art Unit

1636

Page 1 of 2

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*	Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
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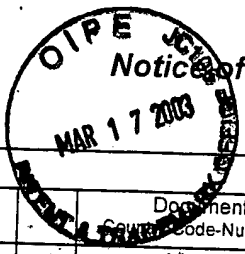
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Application/Control No. 09/900,497		Applicant(s)/Patent Under Reexamination ALLEN, KEITH D.	
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Date: October 26, 2001


Serial No.:  
09/900,497

Filing Date:  
**July 6, 2001**

Group Art Unit: 1614

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INFORMATION DISCLOSURE CITATION  
PTO-1449

SHEET 2 OF 4

TRANSGENIC MICE CONTAINING NPY6-R  
NEUROPEPTIDE GENE DISRUPTIONS

Date: October 26, 2001

Atty Docket:  
R-639

Serial No.:  
09/900,497

Applicant:  
ALLEN

Filing Date:  
July 6, 2001

Group Art Unit: 1614

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**INFORMATION DISCLOSURE CITATION**  
 PTO-1449

**TRANSGENIC MICE CONTAINING NPY6-R  
NEUROPEPTIDE GENE DISRUPTIONS**

Date: October 26, 2001

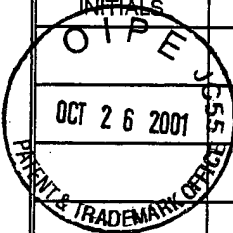
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 Applicant:  
**ALLEN**

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